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WORKING MEMORY DEPENDENT PREFRONTAL-PARIETAL CONNECTIVITY AND MODEL-BASED DIAGNOSTIC CLASSIFICATION IN SCHIZOPHRENIA

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Impaired working memory (WM) is among the best-established findings in schizophrenia. Nevertheless, functional neuroimaging studies on WM yielded inconsistent results. Disrupted functional integration in the WM network may explain neural inefficiency more precisely. This so-called ´dysconnectivity´-hypothesis of schizophrenia focuses on abnormal synaptic plasticity.
In a step towards pathophysiologically informed diagnostic classification schemes, the recent introduction of “generative embedding” procedures to neuroimaging offers the combination of neurobiologically interpretable generative models (e.g. DCMs) and support vector machines (SVM) for diagnostic classification.
This fMRI study in 41 schizophrenia patients and 42 healthy controls presents four major results:
1) Across controls and patients, prefrontal activation is modulated by WM performance resulting in an inverted U-curve.
2) DCM of the prefrontal-parietal WM network demonstrated that WM-dependent prefrontal to parietal connectivity is reduced in all patients independent of WM performance.
3) Classification in a supervised setting using generative embedding yielded 78% accuracy. Using model-based clustering in an unsupervised fashion performed almost equally well (71% accuracy).
4) Subclustering schizophrenia patients revealed three distinct subgroups of patients. These subgroups exhibited different profiles of prefrontal-parietal connectivity and, critically, were found to differ significantly in clinical symptoms.
This study reveals putative mechanisms underlying prefrontal inefficiency and cognitive deficits in schizophrenia, providing direct experimental evidence for the dysconnectivity hypothesis. A novel model-based clustering approach revealed three distinct subgroups of patients with unique connectivity profiles and significant differences in clinical ratings. This translational approach may help to identify specific factors underlying the variability of treatment responses and to develop subgroup-specific treatment approaches.

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